BASF

December 30, 1996

Engineering & Ecology

California Air Resources Board
2020 L Street
Sacramento, CA 95812

Dear Sirs:

This correspondence is in response to the decision by the EPA to remove caprolactam from the Clean Air Act section 112 hazardous air pollutant (HAP) list. BASF Corporation requests the State of California take similar action to remove caprolactam from its hazardous air pollutant list found in Subchapter 7, Section 93001 - Hazardous Air Pollutants Identified as Toxic Air Contaminants which was incorporated from the EPA's original 189 HAP listing.

On June 18, 1996, EPA published in the Federal Register (61 FR 30816) its final decision to delist caprolactam from the Clean Air Act section 112 list of hazardous air pollutants and Clean Air Act requirements that follow such a listing. The EPA arrived at this decision only after an extensive data collection and review process unprecedented in such delisting proceedings. All aspects of the potential hazards from projected exposures to caprolactam were examined prior to EPA concluding that there exists "adequate data on the health and environmental effects of caprolactam to determine that emissions, ambient concentrations, bioaccumulation, or deposition of the compound may not be reasonably anticipated to cause adverse human health or environmental effects."

BASF Corporation is writing all states that have incorporated caprolactam into their air toxic programs, to urge them to consider EPA's process and conclusion and remove it from their programs as well. It appears inappropriate to further require businesses in California to burden the costs of compliance with air toxics regulations in a very competitive market place when the material clearly does not justify such expenditures. BASF Corporation believes such regulations should be reserved for air toxics that truly have a significant risk potential.

Thank you in advance for your consideration of this request. Should you have questions regarding this request or would like to further discuss this issue, please contact me at (704) 667-7742.

Sincerely,

Wendell A. Dickson

Wendell A. Dickson
Corporate Air Team Member

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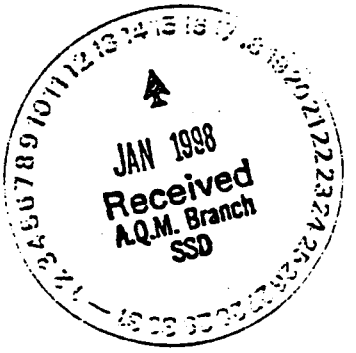
FICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

MEMORANDUM



TO: Genevieve A. Shiroma, Chief
Air Quality Measures Branch
Air Resources Board

VIA: George V. Alexeeff, Chief
Air Toxicology and Epidemiology Section

Melanie A. Marty, Chief
Air Risk Assessment Unit

FROM: James F. Collins
Staff Toxicologist
Air Risk Assessment Unit

DATE: January 8, 1998

SUBJECT REVIEW OF HEALTH EFFECTS OF CAPROLACTAM

We are responding to your request to review the health effects of caprolactam. USEPA removed caprolactam from the Clean Air Act Section 112 hazardous air pollutant list. In a letter dated December 30, 1996, BASF Corporation requested similar action under the Toxic Air Contaminant (TAC) program. Due to the short lead time and the difficulty in accessing the primary literature on caprolactam, we mainly consulted secondary sources such as the Hazardous Substances Data Bank (HSDB, 1997), U.S. EPA's Integrated Risk Information System (IRIS) (USEPA, 1997a) and IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans (IARC 1979, 1986). In addition to reviewing the health effects, we have also reviewed the basis of the USEPA's action to delist. We hope that the information below is useful in your determination.

SUMMARY OF HEALTH EFFECTS

Occupational (high level) exposures to caprolactam have been reported to lead to respiratory irritation, contact dermatitis and eczema, headaches, malaise, loss of normal touch sensation in fingertips, loss of control and some confusion, irregular menstruation and pregnancy/birth complications. When administered in large doses to animals, caprolactam is a convulsant poison, a powerful respiratory stimulant, and a mild circulatory depressant. When

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administered to growing animals over long periods, caprolactam tends to cause a mild but reversible growth depression. Caprolactam is considered to have a relatively low toxicity to humans at low levels, attributed in part to its rapid elimination. IARC has determined that caprolactam is probably not carcinogenic to humans (class 4). However, the toxicologic database has substantial gaps. A major data gap is the absence of a lifetime study by the inhalation route. The longest animal inhalation experiment lasted 4 months. The only lifetime animal cancer study used the oral route. U.S. EPA has not been able to find appropriate data to set a reference concentration (RfC) for ambient exposure of humans to caprolactam. No other reference exposure levels are available to ascertain the potential noncancer hazard of likely exposure scenarios. Thus there is uncertainty about the health effects due to chronic inhalation of caprolactam.

GENERAL INFORMATION ON CAPROLACTAM

According to Chemical and Engineering News (1995) 1.36 billion pounds of caprolactam were produced in the US in 1993 and 1.68 billion pounds in 1994. Caprolactam is used in the manufacture of synthetic fibers, especially nylon 6 (polycaprolactam), plastics, bristles, film, coatings, synthetic leather, plasticizers and paint vehicles, as a cross-linking agent for polyurethanes, and in the synthesis of the amino acid lysine. According to the TRI database there were no emissions of caprolactam in California in 1995, the latest reporting year. The ATEDS database also lists no emissions of caprolactam in California.

In a critical review of the literature Gross (1984) summarized his findings: (1) When administered in large doses to animals, caprolactam is a convulsant poison, a powerful respiratory stimulant, and a mild circulatory depressant. (2) When administered to growing animals over long periods, caprolactam tends to cause a mild but reversible growth depression. (3) Caprolactam is considered to have a relatively low toxicity to humans, attributed in part to its rapid elimination.

PHYSICAL AND CHEMICAL PROPERTIES OF CAPROLACTAM (HSDB, 1997)

Molecular formula	$C_6H_{11}NO$
Molecular weight	113.16
Specific gravity	0.843 @ 20°C
Boiling point	180° C @ 50 mm HG
Melting point	70° C
Vapor pressure	6 mm Hg @ 120°C
Solubility	soluble in water, ethanol, benzene, chloroform; freely soluble in methanol, ethanol, tetrahydrofurfuryl alcohol, ether, and dimethylformamide; soluble in cyclohexene and petroleum fractions
Odor and taste	unpleasant
Odor threshold	not established

Metabolite(s)	ε-aminocaproic acid
Description	white crystals
Conversion factor	1 ppm = 4.6 mg/m^3 @ 25° C

ACUTE TOXICITY

Caprolactam has been tested by various routes of exposure. The following lethal concentrations have been reported for the inhalation route:

LC_{50} FROM INHALATION EXPOSURE
Mouse 450 mg/m^3/2 hr (IARC, 1986)
Rat 300 mg/m^3/2 hr (IARC, 1986)

These are equivalent to 98 and 65 ppm, respectively for mice and rats. Thus under Title 22, Social Security, Division 4, Environmental Health, Article 11, Criteria for Identification of Hazardous and Extremely Hazardous Wastes, caprolactam would be classified as extremely hazardous since the inhalation LD_{50} is less than 100 ppm. The LC_{50}s would probably be lower (more potent) at the more standard, longer exposure period of 4 hours.

On direct contact, caprolactam vapors irritate eyes, nasal passages, and skin. People exposed deliberately to several concentrations of caprolactam vapor ranging from 53 mg/m^3 to 521 mg/m^3 confirm that eye irritation is experienced by everyone at these relatively high concentrations (ACGIH, 1986). Dermatoses among workers in a caprolactam manufacturing plant showed that contact dermatitis and eczema of the hands were most prevalent (NRC, 1977). The lesions consisted of dry erythematous (red) squamous foci on smooth skin.

Workers exposed to 61 mg/m^3 and to 16-17 mg/m^3 of ε-caprolactam complained of apprehension and nervous irritability. Other symptoms included bleeding from the nose, dryness of nose, inflammation of the throat, painful lips, heartburn, flatulence, and a bitter taste in the mouth (International Labour Office, 1971). Workers exposed to concentrations of less than 17.5 mg/m^3 complained of headaches and malaise, dry glossy skin, loss of normal touch sensation in fingertips, and nail deformations (International Labour Office, 1971). Loss of control and some confusion were reported to occur in workers exposed to caprolactam. Nervous system, genito-urinary tract, and cardiovascular disorders were observed in female workers exposed to caprolactam during the manufacture of nylon 6 (IARC, 1979). Light sensitivity of the eye was produced by inhalation of caprolactam at 0.11 mg/m^3 and higher (NRC, 1977).

Based on his review of the animal literature, Gross (1984) selected the following no observed effect levels (NOELs) for caprolactam by inhalation:

animal	dose	duration	reference
mice	10 mg/m^3, 4 h/day	4 months	Lomonova, 1966
rats	0.06 mg/m^3	82 days	Krichevskaya, 1968
guinea pigs	118-261 mg/m^3, 7 h/day	7 days	Goldblatt, 1954

The very great difference among species could be real, it could be due to the limited amount of experimentation done, or it could reflect the varying exposure periods. The exposures vary from acute/subacute (7 days) to subchronic/chronic (4 months).

GENETIC TOXICITY (HSDB, 1997)

Twenty-seven chemicals (including caprolactam), previously tested in rodent carcinogenicity assays, were tested for induction of chromosomal aberrations and sister chromatid exchanges in Chinese hamster ovary cells as part of a larger analysis of the correlation between results of in vitro genetic toxicity assays and carcinogenicity bioassays. Chemicals were tested up to toxic doses with and without exogenous metabolic activation. Results showed that treatment of the Chinese hamster ovary cells with up to 5 mg/ml caprolactam in the presence or absence of S9 did not increase the frequency of chromosomal aberrations or sister chromatid exchanges. (Gulati et al., 1989)

Caprolactam gave negative results in a wide range of *in vitro* short-term tests. It did not induce mutation in *Salmonella typhimurium* in the presence or absence of an exogenous metabolic system, recombination or aneuploidy in fungi, or DNA damage, DNA repair, point mutation, sister chromatid exchange, micronuclei, aneuploidy or polyploidy in cultured mammalian cells. Results of borderline positivity were obtained in tests for gene conversion in yeast and for morphological transformation in cultured mammalian cells. Caprolactam induced somatic-cell mutations in Drosophila melanogaster. There is some evidence that it induced point mutations in yeast and chromosomal aberrations in cultured human cells (IARC, 1986).

When pregnant Swiss-Webster mice were treated by oral intubation with 6.5-6.7 mg/kg body weight ^{14}C-caprolactam, rapid transfer of the radioactivity across the placenta was demonstrated by whole-body autoradiography, with near-complete elimination from the fetal and maternal compartments 24 h after treatment (IARC, 1986).

In male rats exposed for 4 h per day to 125 mg/m^3 (27 ppm) caprolactam dusts, spermatogenesis was reduced after 2.5 months. No effect was seen in animals exposed to 11 mg/m^3 (2.4 ppm) (IARC, 1986).

CANCER (IARC, 1986)

IARC has classified caprolactam in Group 4, probably not carcinogenic to humans. There was no evidence for its carcinogenicity in experimental animals. The principal study was a National Toxicology Program lifetime (103 weeks) oral study. Male and female Fischer 344/N rats were fed a diet containing 3,750 or 7,500 mg/kg (ppm) caprolactam. Male and female B6C3F1 mice were fed a diet containing 7,500 or 15,000 mg/kg (ppm) caprolactam. No treatment related tumors were detected. For humans, there were no data available.

CHRONIC TOXICITY IN WORKERS (USEPA, 1997a)

The U.S. EPA reviewed the occupational and experimental literature on caprolactam in order to develop a Reference Concentration (RfC) (USEPA, 1997). An RfC is equivalent to an OEHHA chronic reference exposure level (REL). This section is a nearly verbatim reproduction of the information from U.S. EPA's review as presented on IRIS (USEPA, 1997a). After the review, USEPA decided that the data could not be used to develop an RfC.

Ferguson and Wheeler (1973) present retrospective information on occupational exposures to caprolactam. Little actual data on workers are presented, although some earlier corroborative documentation (Ferguson, 1972) shows that medical records of 155 workers (several of whom apparently had worked in the plants for more than 17 years) in two plants were examined for possible indications of reported health effects due to caprolactam over a period of 17 years prior to the study. The search yielded only three cases of skin irritation, all relating to direct exposure to caprolactam. TWA exposures of workers, based on area samples, in various plant locations ranged up to 4.8 ppm (23 mg/m^3).

As an experiment by the same authors, the effects of caprolactam were investigated in five volunteer workers who were stationed at various distances from a caprolactam source, and their subjective complaints were noted after momentary exposure. These workers had not been exposed continuously in their work duties. Irritation associated with caprolactam exposure was characterized as transient, ceasing promptly after termination of exposure. The authors claim a concentration response for these effects because transient irritant effects of the eyes, nose, and throat were noted in workers at 100 ppm with distress decreasing as concentration decreased such that no eye irritation was noted below 25 ppm. The majority (4/5) experienced upper airway irritation at 10 ppm (46 mg/m^3) caprolactam, the lowest concentration tested. Transient nose and throat irritation occurred in some subjects at all levels above 10 ppm, and no distress was noted at concentrations ranging up to about 7 ppm. The authors claim that discomfort from irritation generally was absent in workers located where these lower exposures (<7 ppm) were measured. Reported complaints varied greatly with respect to perceived magnitude of discomfort, however. Somewhat higher discomfort levels were reported from subjects in the polymer plant versus those in the monomer plant. The authors suggest that the higher humidity in the monomer plant may have protected those subjects from the irritant effects of caprolactam by ensuring tissue hydration and biological clearance.

Both components of the study by Ferguson and Wheeler (1973) have significant deficiencies (in terms of data to quantify a dose-response relationship). Neither the number of workers nor the average duration or distribution of exposure are given in the occupational portion of the study. No historical air levels are given, and all exposures are determined from area rather than personal samplers. No attempt to reconstruct individual exposure histories was made. The relationship of some of the supporting data on worker medical and employment records (Ferguson, 1972) to the formal study is not linked clearly. No firm basis exists for consideration of this study as chronic in duration because no definite worker population is present and no average exposure duration is reported. Although judgment about the onset and intensity of irritation is known to have substantial subjective components (OSHA, 1989), only five individuals

were used in the irritation portion of the study and no concentration was examined at which irritation was absent in all. The animal-based evaluation for sensory irritation (Alarie, 1973) provides a more objective measure, although this methodology recently has been criticized (Bos et al., 1992). These deficiencies preclude the use of this study in the derivation of an RfC.

Billmaier et al. (1992) examined medical records of 39 workers from two plants for health effects related to caprolactam exposure. Each of the exposed workers was matched for age, sex, race, and smoking history with at least one control who had not been exposed to caprolactam. Worker selection was also based on a minimum of 10 years work exposure (mean 18.7 +/- 7.0, range 8.2-31.7 years) and the existence of pulmonary function test data for this period. Pulmonary function test data consisted of expiratory spirographs from which forced vital capacity, forced expiratory volume in one second, and other values related to these measures were obtained. Other health record information, available for all shifts from 1980-1991, was examined for worker complaints associated with exposure to caprolactam. Historical industrial hygiene monitoring of one plant indicated caprolactam air concentrations to be 3.7 mg/m^3 and for the areas of highest exposure in the other plant, 4.5 and 9.9 mg/m^3. No personal air samples were taken. In comparing exposed workers and their controls, no statistically significant alterations were noted in any pulmonary function test. Possible detection of a smoking effect indicates that the study may have been sensitive enough to detect pulmonary obstruction. Of 878 worker visits to the medical clinic from 1980-1991, two could be related to direct dermal contact with solid caprolactam, and there was one episode of eye irritation and one episode of inhalation of material possibly containing caprolactam. Although the results from this study suggest that prolonged inhalation exposure to caprolactam vapors at concentrations as high as 9.9 mg/m^3 are without adverse consequence for the lower respiratory tract, the small sample size precludes further conclusions. Furthermore, it appears that the spirometry performed and evaluated in this study was not in accordance with current guidelines (ATS, 1987) and quality assurance procedures (Gardner et al., 1986). Upper respiratory tract symptomatology was not investigated in this report.

Spirometry was performed on 173 caprolactam plant workers who had an average exposure of 12 years (Patel, 1990). After adjusting for age, height, and smoking habits, no differences were noted between the exposed cohort and 60 nonexposed workers. No exposure information was given in this study.

Guirguis (1990) reports on a case control study of six workers who developed respiratory problems within a year after being exposed to a mixture of emissions of which one was caprolactam at 0.46 mg/m^3. The respiratory problems (including symptoms of bronchial hyperreactivity, asthmatic responses, and deficits in pulmonary functions tests) were preceded by eye, nasal, and upper respiratory tract irritation.

Information on human exposure to caprolactam dust is limited. Kelman (1986) reported that workers exposed to caprolactam dust/vapor at 68-84 mg/m^3 for an average of 4.8 years showed evidence of dermal damage but not systemic toxicity. Hohensee (1951) states that worker complaints at the end of an 8-hour work shift where caprolactam vapor/dust was claimed to be present at 61 mg/m^3 included irritability, nervousness, nosebleeds, irritation/inflammation of

the upper respiratory passages, dry nose, abdominal gas, and heartburn. Ferguson and Wheeler (1973) reported that exposure to caprolactam dust produces skin irritation, although no concentrations are given. OSHA and ACGIH both promulgate a TLV-TWA for caprolactam dust of 1 mg/m^3 for avoidance of dermal irritation in workers; this value is 20-fold less than for the vapor.

CHRONIC TOXICITY IN ANIMALS (USEPA, 1997a)

Male albino rats (15/group) were exposed either to air or to 0.06, 0.6, or 6.0 mg/m^3 caprolactam for 82 days (Krichevskaya, 1968). Information regarding length of daily exposure is not given. Alterations in whole blood cholinesterase, "chronaxial ratio," and several biochemical measures were reported to occur in rats exposed to the highest concentration. Effects on cerebral electrical activity in three volunteers also were reported at concentrations as low as 0.11 mg/m^3. Little data is available in this report, and the significance of the results is unclear.

Albino mice (sex not specified) were exposed either to air or to 10 mg/m^3 caprolactam for 4 hours/day for 4 months. Body weights were monitored, various behavioral tests and some pathology were performed. Little data is presented in this study. No effects attributable to caprolactam were reported (Lomonova, 1966).

Alarie and Stock (1990) exposed guinea pigs (groups of four) for 0.5 hours on 5 consecutive days to air or to 3, 10, or 30 mg/m^3 aerosols generated from a 15% aqueous solution of caprolactam. Animals were monitored with whole-body plethysmography for indications of irritation, coughing, pulmonary hypersensitivity, and airway hyperreactivity. No significant respiratory responses were noted during the 5-day repeated exposure period, including sensory or pulmonary irritation, even at the highest concentration. No tissues were examined in this study.

Three successive generations of Fischer 344 rats (20 females and 10 males/generation) were mated after a 10-week dietary exposure to 0, 1000, 5000, or 10,000 ppm (500 mg/kg/day) caprolactam (Serota et al., 1984, 1988). The number of live and dead pups was noted for each litter, with individual body weights and any abnormalities noted on days 1, 7, and 21 of lactation. In pups chosen as parents for the following generations, all reproduction indices were noted. Lower mean body weights (accompanied by concomitant decreases in food consumption) were observed in the P2 and P3 generations of both sexes treated at the highest dose level. All pregnancy and fertility indices were unaffected by caprolactam treatment. There was a consistently lower mean body weight in both female and male pups in all filial generations at both the 10,000 ppm and 5000 ppm (500 and 250 mg/kg/day, respectively), but not at the 1000-ppm dose level (50 mg/kg/day). The results in this study were used in the derivation of the current RfD for caprolactam, 0.5 mg/kg/day.

Pregnant Fischer 344 rats (20/dose group) were intubated with caprolactam at 0, 100, 500, or 1000 mg/kg/day on gestation days 6-15. Dams in the highest dose group experienced mortality (>50%). The mean body weight changes (and food consumption) in the two highest dose groups were less ($p = 0.05$) than controls and the lowest dose group on days 6-11. The mean incidence of resorption in the highest dose group was nearly 10-fold higher in the controls

and all other dose groups. No dose-related malformations or anomalies were noted among the offspring of any exposure group, although skeletal variants (including incomplete ossification of the skull or vertebral column, and the presence of extra ribs) were markedly increased among offspring from animals exposed to the highest dose (Gad et al., 1987). This study identifies a NOAEL of 100 mg/kg/day for developmental effects in rats and an FEL (Frank Effect Level) of 1000 mg/kg/day.

Pregnant New Zealand white rabbits (25/group) were intubated with water or 50, 150, or 250 mg/kg caprolactam/day on gestation days 6-28. Mortality was observed (4/25) in the highest dose group only, and maternal body weight gain was significantly depressed ($p < 0.05$) on gestation days 6-9. Lower mean fetal weights ($p < 0.05$) were noted among fetuses in the two highest dose groups. An increased incidence of unilateral or bilateral thirteenth ribs was noted among fetuses whose mothers had been exposed to the highest concentration of caprolactam (Gad et al., 1987). A NOAEL of 50 mg/kg is identified by this study, with 250 mg/kg being an FEL.

REPRODUCTIVE STUDIES

A number of limited studies exist on reproductive effects in both humans and animals from inhalation of caprolactam vapors/dust. The human studies, many of which have been reviewed by Gross (1984), are confounded due mostly to coexposures. The studies do, however, report effects that are internally consistent with one another and with the animal studies. The numerous deficiencies in these studies in reporting, data presentation, and methods preclude their use in a concentration-response assessment. They do, however, indicate an area of uncertainty on reproductive endpoints (ovarian-menstrual functions and male gonadal parameters) that were not evaluated specifically in the long-term oral studies of NTP (1982) or the three-generation reproductive study of Serota et al. (1988). These studies are described briefly below.

The human occupational studies in which female workers were exposed to caprolactam vapors/dusts consistently report alterations in ovarian-menstrual functions and condition. Nadezhdina and Talakina (1971) (also reported in Livke et al., 1971) report unspecified disturbances in ovarian menstrual function occurring in 37.1% of 170 pregnant workers exposed to caprolactam (no levels given) versus 12.8% in a control population of 101 pregnant women. Petrov (1975) reported that inflammatory diseases of the uterus and "uterine appendages" were more prevalent in a female worker population ($n = 492$) exposed to <10 mg/m^3 caprolactam and biphenyl than in a control population (8.9% versus 1.08%). Martynova et al. (1972) reported a 48.2% incidence of menstrual function disorders, the most frequent being hypomenstrual syndrome, in a group ($n = 300$) of female caprolactam workers; the authors give no exposure levels but do state that this rate was 2.5 times that of the controls. In a cohort of 304 female workers exposed to <10 mg/m^3 caprolactam (no duration given), irregular menstruation was significantly greater than in paired controls (34.3% vs. 25%; $p < 0.005$) (Liu et al., 1988). In a cross-sectional study of 200 female workers exposed to <10 mg/m^3 caprolactam, Angelov (1988) noted that the incidence of uterine myoma (a tumor containing muscle tissue) in a cohort of 616 female workers exposed to a number of compounds including caprolactam, was 2-3 times higher than in a control population of 182 women. Martynova et al. (1972) also claim that pregnancy/birth complications occurred at a higher rate in a group of women ($n = 137$) exposed

to caprolactam than in a group of 150 control women, including hemorrhage at 33.8% in exposed vs. 18.1% in controls.

The animal studies available on inhalation exposure to caprolactam also have numerous deficiencies. The studies are not, however, confounded by coexposure. Khadzhieva (1969a) exposed inseminated female rats either to air (n = 22) or to 139.2 (n = 40) or 473 (n = 46) mg/m^3 caprolactam vapor/dust. The daily duration of exposure was 4 hours, but the number of days is not clearly stated; some animals were exposed during the preimplantation phase, some during the period of organogenesis, and still others during fetal development. The results show concentration responses in the percent impregnated, in alteration of pregnancy duration, in mean birth weights, and in the percent of live-born young (based on corpora lutea). These parameters were clearly different from controls at both exposure levels. In a report apparently conducted on the same animals prior to their insemination, this author reports significant shortening of the rutting stage and prolongation of the dormancy phase of the estrous cycle (assumed to be estrus and diestrus, respectively), the latter effect occurring at both levels of exposure (Khadzhieva, 1969b). Gabpielyan et al. (1975) exposed three groups (number unspecified) of male rats either to air or to 10.6 or 124.6 mg/m^3 caprolactam dust/vapor for 4 hours/day for 2.5 months, and various measures of the gonads were taken at the end of this period. Statistically significant alterations relative to controls ($p < 0.05$) were noted in the spermatogenesis index (unspecified), the total quantity of normal spermatogonia, and the number of tubules at twelfth-stage meiosis in those animals exposed to the higher concentration. No significant alterations relative to controls were noted in those animals exposed to the lower concentration. In an effort to explain his observation of increased uterine hemorrhage during and after birth in female workers exposed to caprolactam, Martynova et al. (1972) showed a reduction in spontaneous uterine contractions in pregnant rabbits after injection with an unspecified volume of a 10% solution of caprolactam.

EXCRETION AND TISSUE DISTRIBUTION

The excretion and tissue distribution of caprolactam has been examined in male Fischer 344 rats after a single oral dose (Unger et al., 1981). By 24 hours post dosing, over 75% of the radiolabel had been excreted in the urine, predominantly as two unidentified metabolites. Small amounts of radiolabel were also present in feces and expired air. Concentration of radiolabel in tissues was substantially the same as blood except for portal-of-entry (stomach) and excretory (bladder and kidney) tissues. Waddell et al. (1984) examined the excretion and tissue distribution of radiolabled caprolactam in male and pregnant female Swiss-Webster mice by whole-body autoradiography. Caprolactam was administered by oral intubation to five pregnant and one nonpregnant female mice and intravenously to two male mice. The radioactivity was distributed throughout the animals (including fetuses) and, by 24 hours, had been nearly eliminated through renal secretion. Small amounts of radioactivity were retained in the cephalic region (including nasal epithelium, optic lens, and olfactory lobe). These data are not suitable for purposes of oral-to-inhalation extrapolation because they are not the appropriate route and provide no information on identity of circulating metabolites. The latter issue may be especially relevant because portal-of- entry tissues capable of metabolism (nasal epithelium) show retention of radiolabeled caprolactam.

Thus, with the literature available, U.S. EPA was not able to set a reference concentration (RfC) for ambient exposure of humans to caprolactam. Therefore, health effects of caprolactam can be identified but a population threshold for ambient exposure cannot be identified. Were caprolactam to be emitted in California, it would be difficult to specify the margin of exposure between the ambient concentration and the threshold for adverse effects.

SUMMARY OF OBSERVED ADVERSE HEALTH EFFECTS

Liver - no effects reported

Kidney -no adverse effects; also, caprolactam is rapidly eliminated by the kidney

Cardiovascular system - mild circulatory depressant at high doses in animals

Respiratory system -respiratory irritant and stimulant

Skin - contact dermatitis and eczema

Nervous system - headaches, malaise, loss of normal touch sensation in fingertips, loss of control and some confusion in workers; light sensitivity of the eye

Immune system - no effects reported

Hormonal (endocrine) system - no effects reported

Reproductive system - irregular menstruation and pregnancy/birth complications in women
altered spermatogenesis in rats

Growth/development - mild, reversible growth suppression in animals
skeletal variants in rats

Carcinogenicity - probably not carcinogenic to humans

ASSESSMENTS BY AUTHORITATIVE BODIES

The U.S. EPA has established an oral RfD for caprolactam of 0.5 mg/kg/day. The critical effect was the reduced body weight in offspring in a three generation reproduction study in rats (Serota et al., 1984).

As indicated above, the U.S. EPA has not established an inhalation RfC for caprolactam.

The U.S. EPA has classified caprolactam as Group E, with evidence of noncarcinogenicity for humans.

The International Agency for Research on Cancer (IARC) has classified caprolactam in Group 4, probably not carcinogenic to humans.

The State of California has not identified caprolactam as a carcinogen or reproductive toxicant under Proposition 65. However, it is on the list of possible candidates for inclusion in the Proposition 65 prioritization process as a potential developmental toxicant.

The U.S. OSHA permissible exposure limit (PEL) is 1 mg/m^3 for caprolactam dust and 20 mg/m^3 (5 ppm) for caprolactam vapor. OSHA also has 15 minute short term exposure limits (STELs) of 3 mg/m^3 for caprolactam dust and 40 mg/m^3 (10 ppm) for caprolactam vapor

The U.S. National Institute of Occupational Safety and Health (NIOSH) recommends a 10 hour time weighted average concentration of 1 mg/m^3 for exposure to caprolactam dust and a 15 minute short term exposure limit (STEL) of 3 mg/m^3 for exposure to caprolactam dust.

The American Conference of Governmental Industrial Hygienists recommends a Threshold Limit Value Time Weighted Average (TLV-TWA) of 1 mg/m^3 for caprolactam dust to reduce the potential for irritation of the skin (especially when wearing respirators) and 23 mg/m^3 (5 ppm) for caprolactam vapor, also to reduce the potential for irritation.

The German government recommended a maximal allowable concentration (MAC) for workers of 25 mg/m^3 (Henschler, 1969). (Volunteers experienced mucous membrane irritation at concentrations greater then 50 mg/m^3.)

NIOSH has not developed an IDLH (Immediately Dangerous to Life or Health) concentration for caprolactam.

The National Academy of Sciences has not established a one-hour or 24-hour inhalation Emergency Exposure Guidance Level (EEGL) for caprolactam.

POTENTIAL FOR EXPOSURE

With respect to the Air Toxics "Hot Spots" Program, ATES has not received any exposure or facility risk assessment emissions data on which to assess the potential for exposure of the public. The existing risk assessment guidelines developed by the California Air Pollution Control Officers Association (CAPCOA) do not provide an acute or a chronic Reference Exposure Level for caprolactam for use in facility risk assessments prepared for the Air Toxics "Hot Spots" Program, thus facilities have not provided the relevant data. OEHHA also has not evaluated caprolactam in the development of the SB1731 Air Toxics Hot Spots Risk Assessment Guidelines, Part III, Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. The ARB's Air Toxics Emissions Database (ATEDS) indicates no emissions of caprolactam in California (K. Rosenkranz, personal communication) and the USEPA Toxic Releases Inventory (TRI) indicates no emissions in California. Since reference levels were not available, the ATEDS database emissions may reflect underreporting. However, one Hot

Spots facility in San Bernardino County reported that it used caprolactam and one facility in Los Angeles County reported that caprolactam was present at the facility.

There is a need for reliable exposure assessment information and modeling when evaluating whether or not stationary sources could release caprolactam in ways which could potentially harm the public health. If there are potential releases and exposure estimates become available, a risk characterization can be done.

FEDERAL ACTION ON CAPROLACTAM (http://www.epa.gov/ttn/uatw/atwsmod.html)

Section 112 of the Act contains a mandate for U.S. EPA to evaluate and control emissions of hazardous air pollutants. Section 112(b)(1) includes an initial list of hazardous air pollutants that is composed of specific chemical compounds and compound classes to be used to identify source categories for which the U.S. EPA will promulgate emissions standards. The listed categories are subject to emission standards subsequently developed under Section 112. The U.S. EPA must periodically review the list of hazardous air pollutants and, where appropriate, revise this list by rule. In addition, any person may petition U.S. EPA under Section 112(b)(3) to modify the list by adding or deleting one or more substances. A petitioner seeking to delete a substance must demonstrate that there are adequate data on the health and environmental effects of the substance to determine that emissions, ambient concentrations, bioaccumulation, or deposition of the substance may not reasonably be anticipated to cause any adverse effects to human health or the environment. To demonstrate the burden of proof, a petitioner must provide a detailed evaluation of the available data concerning the substance's potential adverse health and environmental effects, and estimate the potential exposures through inhalation or other routes resulting from emissions of the substance.

On July 19, 1993, U.S. EPA received a petition from Allied Signal, Inc., BASF Corporation, and DSM Chemicals North America, Inc. to delete caprolactam (CAS No. 105-60-2) from the hazardous air pollutant list in Section 112(b)(1), 42 U.S.C., Section 7412(b)(1). A Notice of Receipt was published (58FR45081, August 26, 1993) noting that the data filed were adequate to support decision making. After a comprehensive review of the data submitted, the U.S. EPA published a proposal to delist caprolactam (60FR48081, September 18, 1995). In order to help address public concern, on March 13, 1995, U.S. EPA executed two detailed agreements with Allied Signal concerning the Irmo, South Carolina manufacturing facility and another facility located in Chesterfield, Virginia, copies of which are included in the public docket for this rulemaking. Allied Signal agreed that, if caprolactam was delisted pursuant to the proposal, Allied Signal would install emissions controls which U.S. EPA believed would be equivalent to the controls which would have been required had U.S. EPA issued a standard to control these sources under Section 112. The agreed emissions controls are incorporated in federally enforceable operating permits for the affected facilities, and will be in place years earlier than controls would have otherwise been required. In addition, Allied Signal has agreed to establish a citizen advisory panel concerning the Irmo facility in order to improve communications with the community and to assure that citizens have an ongoing role in implementation of the agreed emission reductions. The public requested a public hearing. On November 28, 1995, the U.S. EPA published a notice of public hearing and an extension of the comment period

(60FR58589). After considering all public comments, the U.S. EPA published a final rule delisting caprolactam (61FR30816, June 18, 1996).

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